Targeting Homologous Recombination Repair In Cancer Cells

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Stellingen behorend bij het proefschrift

Targeting Homologous Recombination Repair In Cancer Cells

1. Inhibition of cell cycle regulatory kinases blocks proliferation as well as DNA repair capacity of cancer cells and thereby is a molecular tool to improve cancer treatment. *(this thesis)*

2. Based on preclinical findings Wee1 inhibition combined with standard radio/chemotherapy is a potential attractive therapeutic option for a subset of cervical cancer patients. *(this thesis)*

3. The identification of FEN1 as a novel homologous recombination (HR) regulator based on transcriptional co-regulation shows that genes with analogous function are likely to be similarly regulated. *(this thesis)*

4. ATR and CHEK1 can be considered Achilles' heels in genomically instable cancer cells such as homologous recombination (HR)-defective cancers and therefore constitute potential therapeutic targets for these cancers. *(this thesis)*

5. Given the observation that defective homologous recombination (HR) can be the result of many different aberrations, testing for HR-deficiency should be ideally based on functional analysis rather than mutational analysis of *BRCA1* and *BRCA2*.
   (Roy et al, Nature Reviews Cancer, 2012; Willers et al, Molecular Cancer Research 2009)

6. In mitotic cells the DNA damage response is rather re-wired than diminished, therefore optimal tumor cell kill requires the combination of mitotic inhibitors and genotoxic drugs.
   (Giunta et al, The Journal of Cell Biology, 2010; Orthwein et al, Science, 2014; Lee et al, Molecular Cell, 2014)

7. A genomically informed choice of cell line models is required to bridge the gap between *in vitro* preclinical studies and clinical studies. *(Domcke et al, Nature Communications, 2013)*

8. No matter how counterintuitive it may seem, basic research has proven over and over to be the lifeline of practical advances in medicine. Without advances, medicine regresses and reverts to witchcraft. *(Arthur Kornberg)*

9. Conducting research is just like cooking, it requires advance planning, creating the best recipe, collecting great ingredients and finally making something you love.

10. After all, science is essentially international, and it is only through lack of the historical sense that national qualities have been attributed to it.
    (Maria Skłodowska-Curie)

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